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Brief Report

Child and Adolescent Psychiatrists' Attitudes and Practices Prescribing Second Generation Antipsychotics

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Abstract

Objective: The purpose of this study was to examine psychiatrists' attitudes and practices in prescribing second-generation antipsychotics (SGA) to children and adolescents (referred to here as ''children'') and identify factors associated with off-label SGA use.

Methods: A survey was mailed to a national, randomly selected sample of 1600 child and adolescent psychiatrists identified by the American Medical Association. Multivariable logistic regression was used to identify factors, including psychiatrists' characteristics, practice characteristics, and psychiatrists' attitudes, that are associated with off-label SGA use (i.e., SGAs used in children with attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder, conduct disorder, or nonbipolar mood disorders).

Results: The final sample included 340 psychiatrists. Overall, respondents reported higher use and appropriateness of SGAs for United States Food and Drug Administration (FDA)-approved disorders, symptoms of aggression, and older child age. More than one third (36%) of respondents reported some off-label SGA use. Significant predictors of off-label use were: Practicing at inpatient/residential facilities (odds ratio [OR] = 4.2, $p = 0.001$); white/non-Hispanic race/ethnicity (OR = 0.3, $p < 0.0001$), agreeing that SGAs should be used for ADHD with aggression (OR = 7.1, $p < 0.0001$); and agreeing that SGAs should be used for severe delinquent behaviors (OR = 1.9, $p = 0.03$).

Conclusions: Psychiatrists' attitudes about prescribing SGAs to children exhibiting aggressive symptoms were associated with off-label SGA use. Research is needed to understand the construct of aggression, potential interaction effects of aggression with diagnostic criteria, and their impact on SGA use.

Introduction

Research over the last decade indicates increasing use of second-generation antipsychotics (SGA) among children and adolescents (hereafter referred to as ''children'') (Olfson et al. 2012; Birnbaum et al. 2013). Increased use partially reflects a growing evidence base and subsequent United States Food and Drug Administration (FDA) approval for psychotic or manic symptoms associated with schizophrenia and bipolar disorder and for aggressive symptoms associated with autism spectrum disorders (ASD) (Agency for Healthcare, Research and Quality 2010). There also has been increased off-label SGAs use among children with attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder (CD), and nonbipolar mood disorders (Shekelle et al. 2007; Crystal et al. 2009), despite limited evidence of efficacy and documentation of cardiometabolic side effects (Correll et al. 2010; Maayan and Correll 2011).

Aggression occurs frequently in children with ADHD, ODD, CD, and nonbipolar mood disorders, and is considered the leading reason worldwide for psychotropic medication use in children (Jensen et al. 2007). Although the construct of aggression is not fully agreed upon, it is associated with a number of diagnoses. Early research focused on physical aggression, whereas recent research has highlighted symptoms of impulsive aggression (e.g., being ''touchy'', ''oppositional'') and other nonspecific behaviors (e.g.,

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''explosive outbursts'') that occur outside of expected social and developmental contexts (Scotto Rosato et al. 2012).

We conducted a survey of child and adolescent psychiatrists to examine attitudes and practices in prescribing SGAs. Specifically, we looked at factors associated with off-label SGA use, including psychiatrists' characteristics, practice characteristics, and psychiatrists' attitudes.

Methods

Using the American Medical Association's (AMA) mailing list, 6156 child and adolescent psychiatrists were identified from which 1600 were randomly selected. Eligibility criteria were: 1) Providing care for children 3–18 years of age, and 2) specializing in child and/or adolescent psychiatry. Psychiatrists who were not based in the United States, were retired, or were residents/fellows were excluded. Of 362 respondents (24%), 94% met eligibility criteria, yielding a final sample of 340.

Data were collected using a survey developed by study investigators. Sections included 1) psychiatrist and practice setting characteristics, 2) self-reported rate of prescribing SGAs by child age and disorder, 3) appropriateness of SGA use by age and symptoms, including aggression, and 4) attitudes toward SGAs and behavioral interventions for aggression. The institutional review board (IRB)-approved survey was mailed twice at 3 week intervals, from February to March 2012.

Means, standard deviations (SD), frequencies, and percentages were used to describe the sample, rate of SGA use ($>50\%$ versus $\leq 50\%$ of the time), appropriateness of SGA use (moderate/very appropriate versus minimal/not appropriate), and attitudes toward SGA use and behavioral interventions for aggression (moderately/strongly agree versus moderately/strongly disagree). We used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CI) of off-label SGA use (i.e., ADHD, ODD, CD, or nonbipolar mood disorders). The following covariates were tested in univariate analysis: Years in practice, respondent race/ethnicity (white/non-Hispanic versus other), respondent gender, board certification in child and adolescent psychiatry, population density where respondent was based, practice setting (inpatient/residential facility versus other), $\geq 50\%$ versus $<50\%$ of patients with private insurance, and attitudes toward SGAs and behavioral interventions for aggression. Covariates with $p<0.2$ were considered in multivariable modeling; backwards selection eliminated variables with $p<0.1$. Multicollinearity was assessed using variance inflation factors (VIF). Alpha was set at 0.05 and tests were two sided; SAS version 9.3 (Cary, NC) was used.

Results

Among the final sample of 340, slightly over half (55%, $n=185$) were male and 71% ($n=236$) were white/non-Hispanic. Respondents' mean age was 53 years (SD = 12) and mean years in practice was 18 (SD = 11). The most common practice setting was private (42%, $n=139$), then community mental health center (24%, $n=80$), academic medical center (16%, $n=51$), inpatient/residential facility (12%, $n=38$), and other (6%, $n=20$). Respondents reported working in urban (48%, $n=157$), suburban (41%, $n=132$), and rural settings (11%, $n=35$). Approximately half (46%, $n=140$) reported that $\geq 50\%$ of their patients had private insurance.

Reported SGA use was high for FDA-approved indications and increased with child age, reaching 73% for adolescents with schizophrenia (Table 1). Nevertheless, 36% ($n=130$) reported some off-label SGA use. Respondents reported low off-label SGA use for ADHD across all ages ($\leq 4\%$). For ODD/CD (7–19%) and

Table 1. Reported SGA Use and Appropriateness of SGA Use by Age Group

	Age 3–5 *% (num/denom)*[c]	*Age 6–12* *% (num/denom)*[c]	*Age 13–18* *% (num/denom)*[c]
Reported SGA use by disorders[a]			
FDA-approved indications			
Schizophrenia	16.3% (33/202)	47.2% (119/252)	72.7% (218/300)
Bipolar disorder	17.5% (44/252)	36.3% (114/314)	64.2% (210/327)
Autism spectrum disorders	17.1% (52/305)	30.8% (99/322)	40.0% (130/325)
Off-label uses			
Mood disorders	11.3% (33/291)	16.7% (53/318)	24.7% (82/332)
Disruptive behavior disorders (CD, ODD)	7.3% (22/301)	11.9% (38/320)	18.5% (60/325)
ADHD/ADD	4.0% (12/300)	1.9% (6/319)	2.5% (8/326)
Appropriateness of SGA use by symptoms[b]			
Target symptoms of disorders			
Has auditory hallucinations	56.4% (186/330)	87.0% (288/331)	94.3% (315/334)
Has sudden mood changes	15.1% (50/331)	39.0% (130/333)	55.9% (186/333)
Acts as if ''driven by a motor''	2.7% (9/332)	8.5% (28/331)	9.9% (33/333)
Aggressive symptoms			
Physically harms or hurts self on purpose	35.4% (117/331)	49.3% (164/333)	59.0% (197/334)
Is explosive or easily angered	16.9% (56/331)	39.8% (132/332)	53.5% (177/331)
Has prolonged temper tantrums	15.8% (52/329)	32.9% (110/334)	50.0% (167/334)
Destroys property	19.1% (63/330)	31.3% (104/332)	40.0% (134/335)
Gets into fights without thinking	9.4% (31/329)	25.5% (85/333)	39.0% (130/333)
Threatens people verbally	8.2% (27/328)	22.6% (75/332)	32.4% (108/333)

[a]Reported use includes prescribing SGAs >50% of the time.
[b]Appropriateness includes both moderately and very appropriate.
[c]Numerator and denominator provided for each response as denominator varied by age (i.e., option to select ''not seen in my practice'').
SGA, second-generation antipsychotic; num, numerator; denom, denominator; CD, conduct disorder; ODD, oppositional defiant disorder; ADHD, attention-deficit/hyperactivity disorder.

nonbipolar mood disorders (11–25%), reported SGA use was also lower, but increased with child age.

Respondents indicated the highest levels of appropriateness of SGA use for symptoms related to schizophrenia (i.e., auditory hallucinations, Table 1). For classic ADHD symptoms (i.e., ''driven by a motor'') few respondents considered SGA use appropriate for any age group (≤10%). Conversely, relatively high proportions of respondents considered SGA use appropriate for symptoms associated with physical and impulsive aggression.

Almost one fifth (19%, $n=64$) agreed that SGAs were the best initial medication treatment for children taking stimulants for ADHD who exhibited aggressive symptoms, and 29% ($n=96$) agreed that SGAs were the best initial medication treatment for children exhibiting severe delinquent behaviors (e.g., assault, destruction of property). In contrast, 68% ($n=226$) agreed that SGAs were the best initial medication treatment for children with ASD exhibiting aggressive symptoms. Regarding behavioral interventions, whereas 43% ($n=144$) agreed that the majority of families could implement the interventions to manage the child's aggression, 40% ($n=133$) agreed that there was difficulty accessing behavioral interventions for patients on psychotropic medications.

On multivariable logistic regression (Table 2), respondents practicing at inpatient/residential facilities were more likely to report off-label SGA use (OR = 4.2; 95% CI = 1.8, 10.2; $p=0.001$). Respondents were more likely to report off-label SGA use if they agreed that SGAs were the best initial medication treatment for children taking stimulants for ADHD who exhibited aggressive symptoms (OR = 7.1; 95% CI = 3.4, 15.0; $p<0.0001$) or agreed that SGAs were the best initial medication treatment for children exhibiting severe delinquent behaviors (OR = 1.9; 95% CI = 1.1, 3.6; $p=0.03$). White/non-Hispanic respondents were less likely to report off-label SGA use (OR = 0.3; 95% CI = 0.2, 0.5; $p<0.0001$). There was no evidence of multicollinearity (VIFs < 1.2).

Discussion

Our results indicate that one third of psychiatrists reported off-label SGA use. Findings suggest several explanatory factors. First, psychiatrists providing care at inpatient/residential facilities predictably used SGAs for off-label indications, likely reflecting increased severity of illness in children treated in those facilities. Second, psychiatrists who agreed that SGAs should be used for aggression with ADHD and severe delinquent behaviors were more likely to report off-label SGA use. Access to behavioral interventions and parental ability to implement them were not included in the model based on univariate analyses. We did not ascertain whether respondents tried behavioral interventions prior to, or simultaneously with, SGAs.

Although the appropriateness of SGA use for different symptoms closely tracked associated disorders, aggressive symptoms appeared to be strongly associated with SGA use. Interestingly, psychiatrists reported similar levels of appropriateness for aggression symptoms as for sudden mood changes. In the absence of a

Table 2. Univariate and Multivariable Logistic Regression for Off-Label SGA Use in Children and Adolescents

	Univariate		*Multivariable*	
	OR (95% CI)	p *value*	*OR (95% CI)*	p *value*
Psychiatrist characteristics				
Male	0.76 (0.48, 1.21)	0.25		
Race/ethnicity				
White/non-Hispanic	0.32 (0.20, 0.53)	<0.0001	0.28 (0.16, 0.51)	<0.0001
Other (reference)				
Board certified in child and adolescent psychiatry	0.55 (0.32, 0.93)	0.03		
Years in practice	0.97 (0.95, 0.99)	0.009	0.97 (0.94, 0.99)	0.009
Practice characteristics				
Practice setting				
Inpatient/residential facility	2.85 (1.31, 6.22)	0.009	4.24 (1.76, 10.18)	0.001
Other (reference)				
Over 50% of patients have private insurance	0.70 (0.43, 1.13)	0.14		
Population density				
Urban (reference)				
Suburban	0.81 (0.49, 1.34)	0.41		
Rural	0.67 (0.30, 1.51)	0.33		
Psychiatrist attitudes				
SGAs best initial treatment for aggression in those on stimulants for ADHD[a]	4.36 (2.42, 7.84)	<0.0001	7.08 (3.35, 14.99)	<0.0001
SGAs best initial treatment for aggression in those with ASD[b]	2.72 (1.56, 4.73)	0.0004		
SGAs best initial treatment for those who exhibit severe delinquent behaviors[c]	2.61 (1.57, 4.33)	0.0002	1.94 (1.05, 3.59)	0.03
Difficult to access behavior interventions for patients on psychotropic drugs[d]	1.21 (0.76, 1.93)	0.42		
Majority of families can implement behavioral strategies to manage aggression[e]	0.83 (0.52, 1.32)	0.43		

[a]SGAs are the best initial medication treatment for children who exhibit aggressive symptoms who are already taking stimulants for ADHD.
[b]SGAs are the best initial medication treatment for children who exhibit aggressive symptoms and have an ASD.
[c]SGAs are the best initial medication treatment for children who exhibit severe delinquent behaviors (e.g., assault, destruction of property).
[d]It is difficult to access behavioral interventions for the majority of my patients who are on psychotropic medication.
[e]The majority of my patients' families can implement behavioral strategies to manage their child's aggression.
SGA, second-generation antipsychotic; ADHD, attention-deficit/hyperactivity disorder; ASD, autism spectrum disorder.

strong evidence base, expert guidelines for the management of aggression for children in inpatient and outpatient settings are available to guide practice; however, it remains critical to conduct ongoing comparative effectiveness studies of those guidelines (Pappadopulos et al. 2003; Schur et al. 2003; Pappadopulos et al. 2011; Knapp et al. 2012; Scotto Rosato et al. 2012).

Limitations

This study has some limitations. The low response rate and inability to compare respondents and nonrespondents limits generalizability. However, our response rate parallels that of other surveys conducted using the AMA mailing list (Needle et al. 2012) and the gender and age distribution match those of other studies of child and adolescent psychiatrists (Association of American Medical Colleges: Center for Workforce Studies 2008). Given that the survey was developed specifically for this study, some factors that may explain SGA use, such as the additive or synergistic impact of overlapping symptoms, were not assessed.

Clinical Significance

Psychiatrists' attitudes about prescribing SGAs to children exhibiting aggressive symptoms were associated with off-label SGA use. Given that aggression is not associated with a single disorder, further research is needed to understand the construct of aggression, potential interaction effects of aggression with diagnostic criteria, and their respective impact on SGA use.

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